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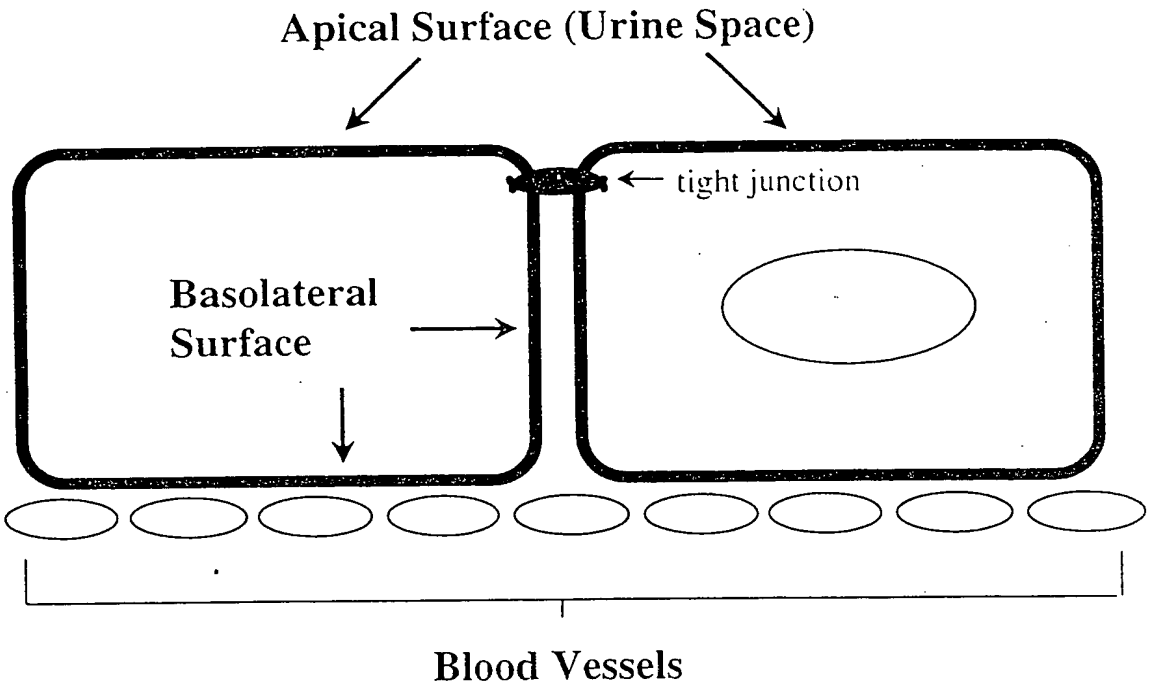
Apical Surface (Urine Space)
tight junction
Basolateral Surface
Blood Vessels

FIG.1

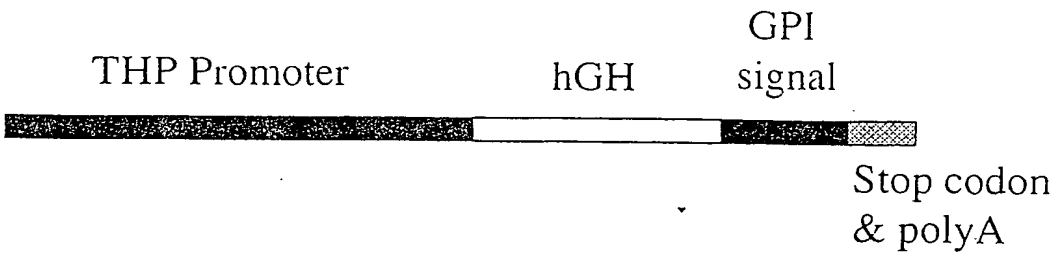
GPI
THP Promoter
hGH
signal
Stop codon
& polyA

FIG.2

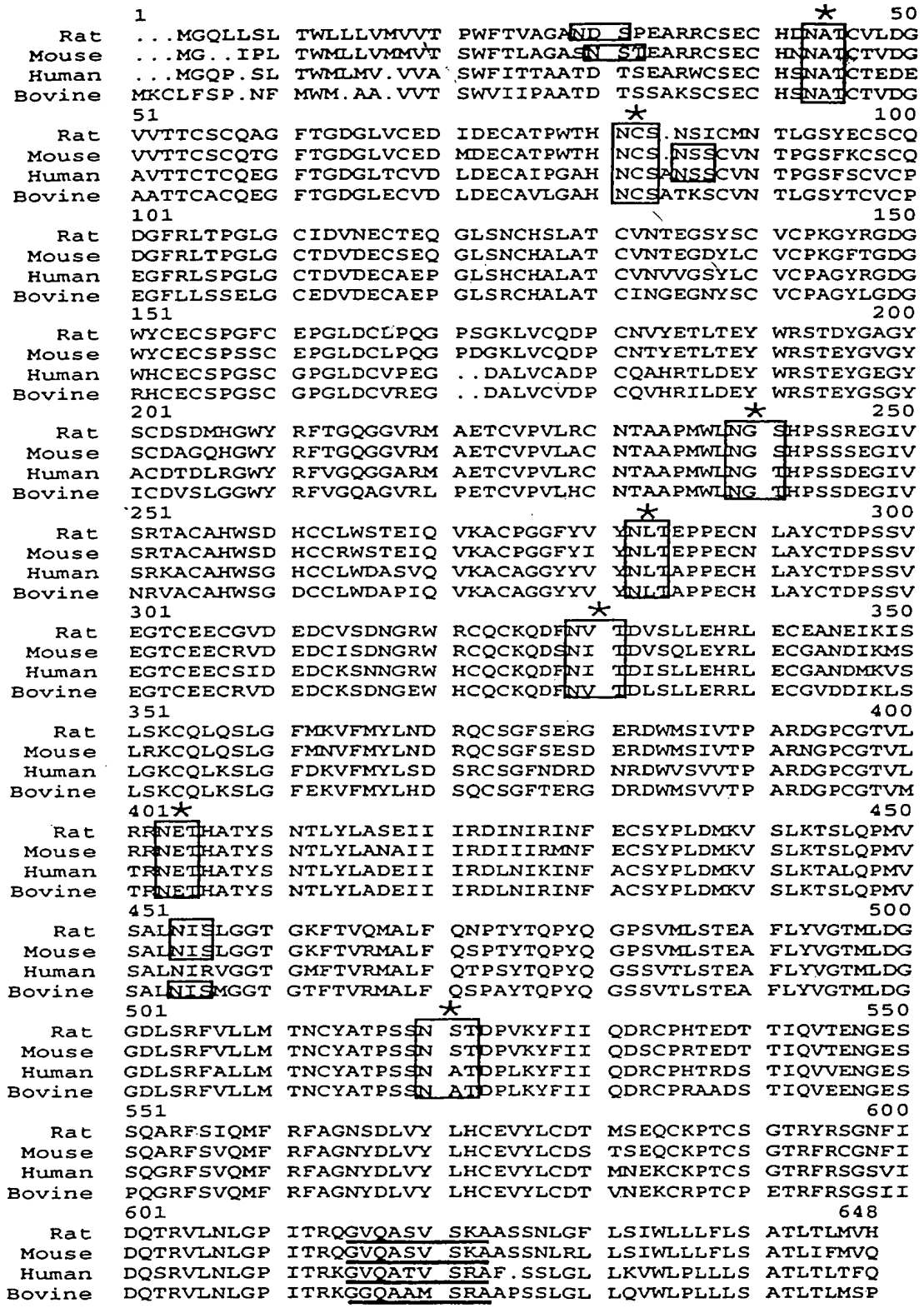
1 50
Rat ...MGQLLSL TWLLLVMVVT PWFTVAGAND SPEARRCSEC HLNATCVLDG
Mouse ...MG..IPL TWMLLVMMVT SWFTLAGASN STEARRCSEC HNNATCTVDG
Human ...MGQP.SL TWMLMV.VVA SWFITTAATD TSEARWCSEC HSNATCTEDE
Bovine MKCLFSP.NF MWM.AA.VVT SWVIIPAATD TSSAKSCSEC HSNATCTVDG
51 100
Rat VVTTCSCQAG FTGDGLVCED IDECATPWTH NCS.NSICMN TLGSYECSCQ
Mouse VVTTCSCQTG FTGDGLVCED MDECATPWTH NCS.NSSCVN TPGSFKCSCQ
Human AVTTCTCQEG FTGDGLTCVD LDECAIPGAH NCSANSSCVN TPGSFSCVCP
Bovine AATTCACQEG FTGDGLECVD LDECAVLGAH NCSATKSCVN TLGSYTCVCP
101 150
Rat DGFRLTPGLG CIDVNECTEQ GLSNCHSLAT CVNTEGSYSC VCPKGYRGDG
Mouse DGFRLTPGLG CTDVDECSEQ GLSNCHALAT CVNTEGDYLC VCPKGFTGDG
Human EGFRLSPGLG CTDVDECAEP GLSHCHALAT CVNVVGSYLC VCPAGYRGDG
Bovine EGFLLSSELG CEDVDECAEP GLSRCHALAT CINGEGNYSC VCPAGYLGDG
151 200
Rat WYCECSPGFC EPGLDCLPQG PSGKLVCQDP CNVYETLTEY WRSTDYGAGY
Mouse WYCECSPSSC EPGLDCLPQG PDGKLVCQDP CNTYETLTEY WRSTEYGVGY
Human WHCECSPGSC GPGLDCVPEG ..DALVCADP CQAHRTLDEY WRSTEYGEGY
Bovine RHCECSPGSC GPGLDCVREG ..DALVCVDP CQVHRILDEY WRSTEYGSGY
201 250
Rat SCDSDMHGWY RFTGQGGVRM AETCVPVLRC NTAAPMWLNG SHPSSREGIV
Mouse SCDAGQHGWY RFTGQGGVRM AETCVPVLAC NTAAPMWLNG SHPSSSEGIV
Human ACDTDLRGWY RFVGQGGARM AETCVPVLRC NTAAPMWLNG THPSSDEGIV
Bovine ICDVSLGGWY RFVGQAGVRL PETCVPVLHC NTAAPMWLNG THPSSDEGIV
251 300
Rat SRTACAHWSD HCCLWSTEIQ VKACPGGFYV YNLTEPPECN LAYCTDPSSV
Mouse SRTACAHWSD HCCRWSTEIQ VKACPGGFYI YNLTEPPECN LAYCTDPSSV
Human SRKACAHWSG HCCLWDASVQ VKACAGGYYV YNLTAPPECH LAYCTDPSSV
Bovine NRVACAHWSG DCCLWDAPIQ VKACAGGYYV YNLTAPPECH LAYCTDPSSV
301 350
Rat EGTCEECGVD EDCVSDNGRW RCQCKQDFNV TDVSLLEHRL ECEANEIKIS
Mouse EGTCEECRVD EDCISDNGRW RCQCKQDSNI TDVSQLEYRL ECGANDIKMS
Human EGTCEECSID EDCKSNNGRW HCQCKQDFNI TDISLLEHRL ECGANDMKVS
Bovine EGTCEECRVD EDCKSDNGEW HCQCKQDFNV TDLSLLERRL ECGVDDIKLS
351 400
Rat LSKCQLQSLG FMKVFMYLND RQCSGFSERG ERDWMSIVTP ARDGPCGTVL
Mouse LRKCQLQSLG FMNVFMYLND RQCSGFSESD ERDWMSIVTP ARNGPCGTVL
Human LGKCQLKSLG FDKVFMYLSD SRCSGFNDRD NRDWVSVVTP ARDGPCGTVL
Bovine LSKCQLKSLG FEKVFMYLHD SQCSGFTERG DRDWMSVVTP ARDGPCGTVM
401 450
Rat RRNETHATYS NTLYLASEII IRDINIRINF ECSYPLDMKV SLKTSLQPMV
Mouse RRNETHATYS NTLYLANAII IRDIIIRMNF ECSYPLDMKV SLKTSLQPMV
Human TRNETHATYS NTLYLADEII IRDLNIKINF ACSYPLDMKV SLKTALQPMV
Bovine TRNETHATYS NTLYLADEII IRDLNIRINF ACSYPLDMKV SLKTSLQPMV
451 500
Rat SALNISLGGT GKFTVQMALF QNPTYTQPYQ GPSVMLSTEA FLYVGTMLDG
Mouse SALNISLGGT GKFTVRMALF QSPTYTQPYQ GPSVMLSTEA FLYVGTMLDG
Human SALNIRVGGT GMFTVRMALF QTPSYTQPYQ GSSVTLSTEA FLYVGTMLDG
Bovine SALNISMGGT GTFTVRMALF QSPAYTQPYQ GSSVTLSTEA FLYVGTMLDG
501 550
Rat GDLSRFVLLM TNCYATPSSN STDPVKYFII QDRCPHTEDT TIQVTENGES
Mouse GDLSRFVLLM TNCYATPSSN STDPVKYFII QDSCPRTEDT TIQVTENGES
Human GDLSRFALLM TNCYATPSSN ATDPLKYFII QDRCPHTRDS TIQVVENGES
Bovine GDLSRFVLLM TNCYATPSSN ATDPLKYFII QDRCPRAADS TIQVEENGES
551 600
Rat SQARFSIQMF RFAGNSDLVY LHCEVYLCDT MSEQCKPTCS GTRYRSGNFI
Mouse SQARFSVQMF RFAGNYDLVY LHCEVYLCDS TSEQCKPTCS GTRFRCGNFI
Human SQGRFSVQMF RFAGNYDLVY LHCEVYLCDT MNEKCKPTCS GTRFRSGSVI
Bovine PQGRFSVQMF RFAGNYDLVY LHCEVYLCDT VNEKCRPTCP ETRFRSGSII
601 648
Rat DQTRVLNLGP ITRQGVQASV SKAASSNLGF LSIWLLLFLS ATLTLMVH
Mouse DQTRVLNLGP ITRQGVQASV SKAASSNLRL LSIWLLLFLS ATLIFMVQ
Human DQSRVLNLGP ITRKGVQATV SRAF.SSLGL LKVWLPLLLS ATLTLTFQ
Bovine DQTRVLNLGP ITRKGGQAAM SRAAPSSLGL LQVWLPLLLS ATLTLMSP

FIG. 3

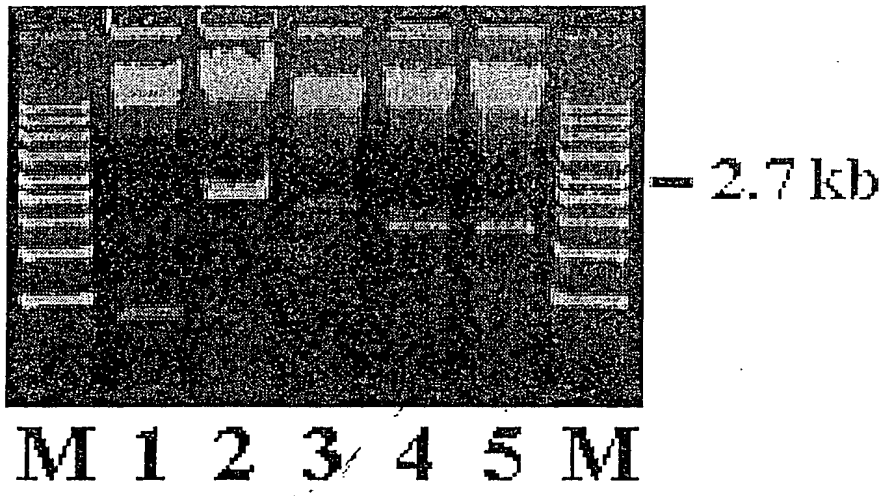

FIG.4

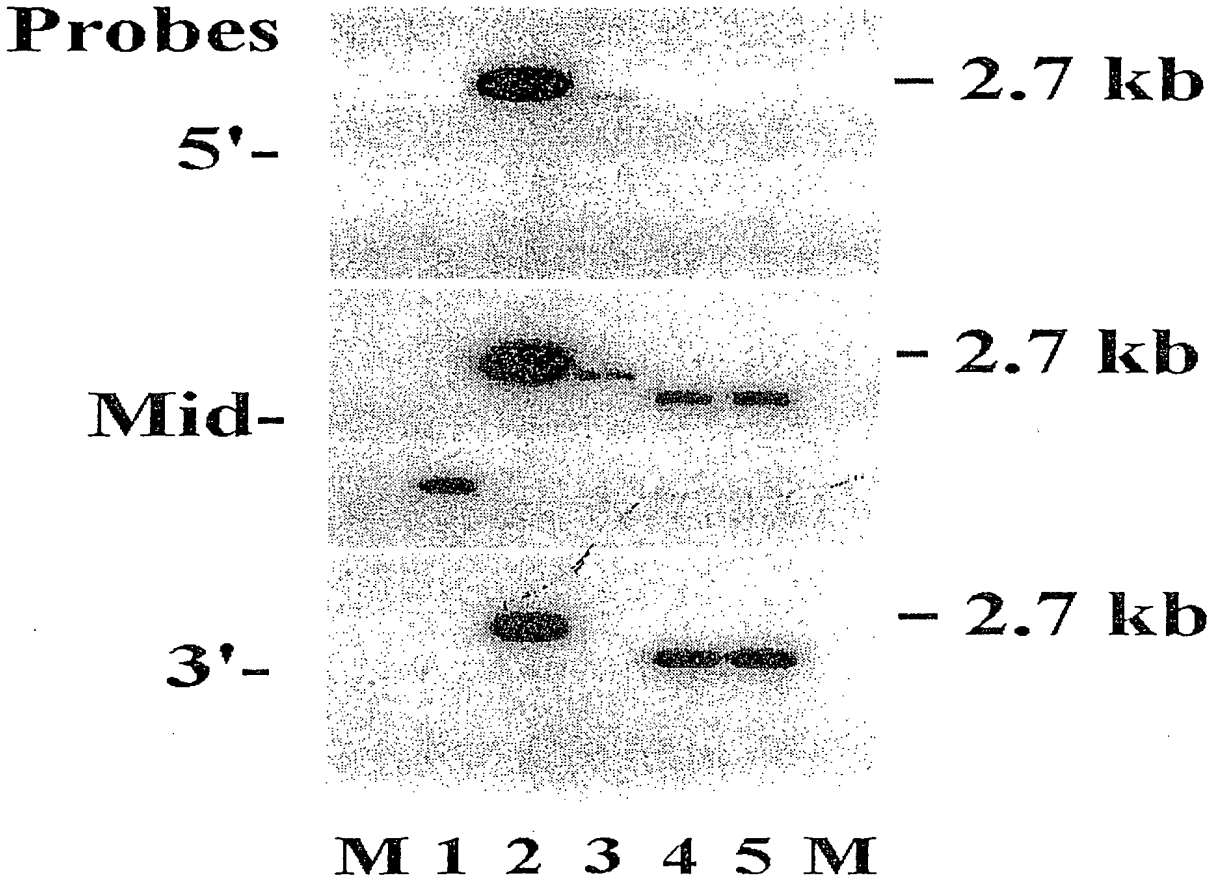

FIG.5

09/08/2004, 09:50:48

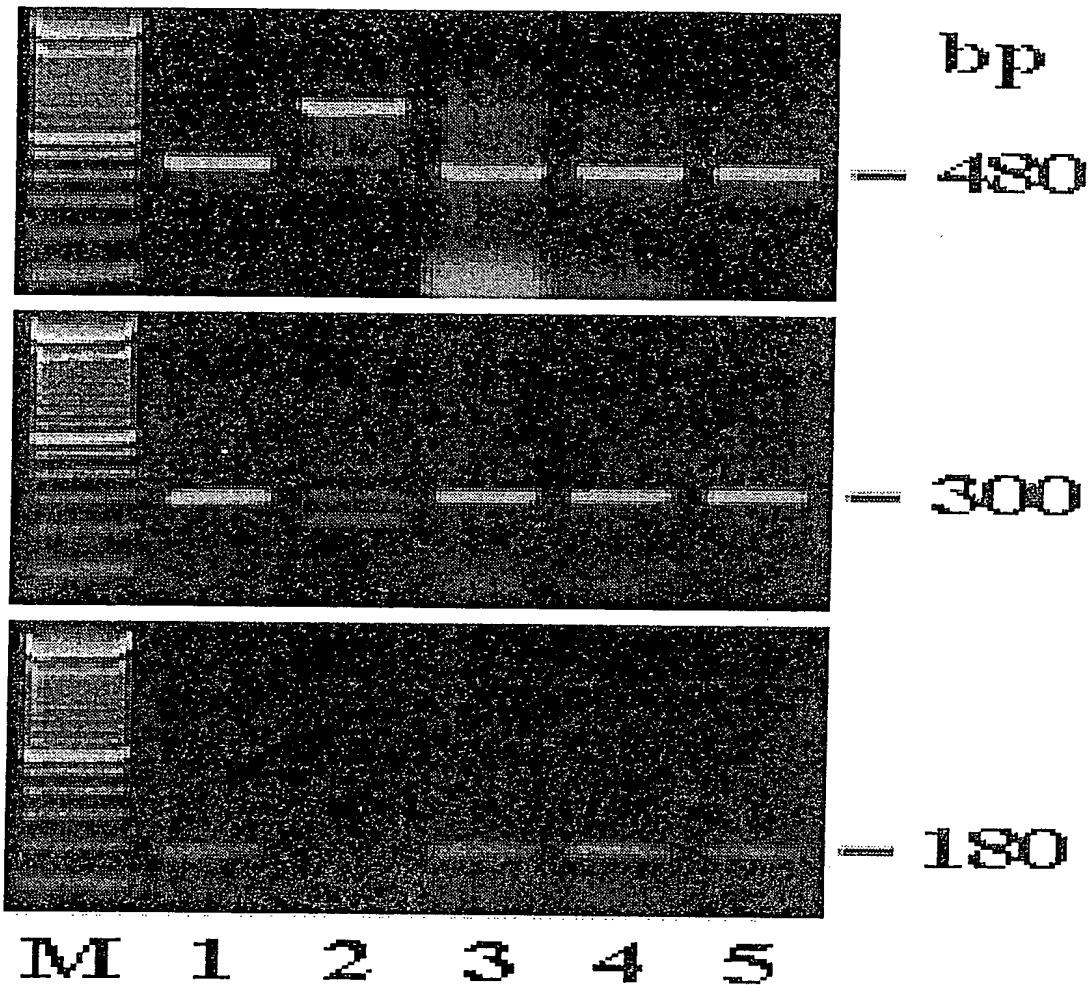

FIG. 6

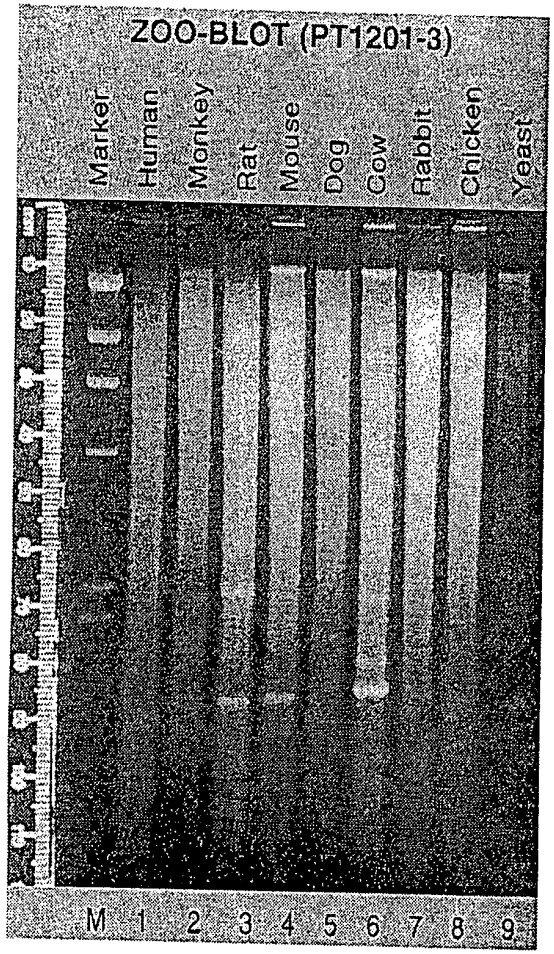
ZOO-BLOT (PT1201-3)
Marker
Human
Monkey
Rat
Mouse
Dog
Cow
Rabbit
Chicken
Yeast
M 1 2 3 4 5 6 7 8 9

FIG. 7A

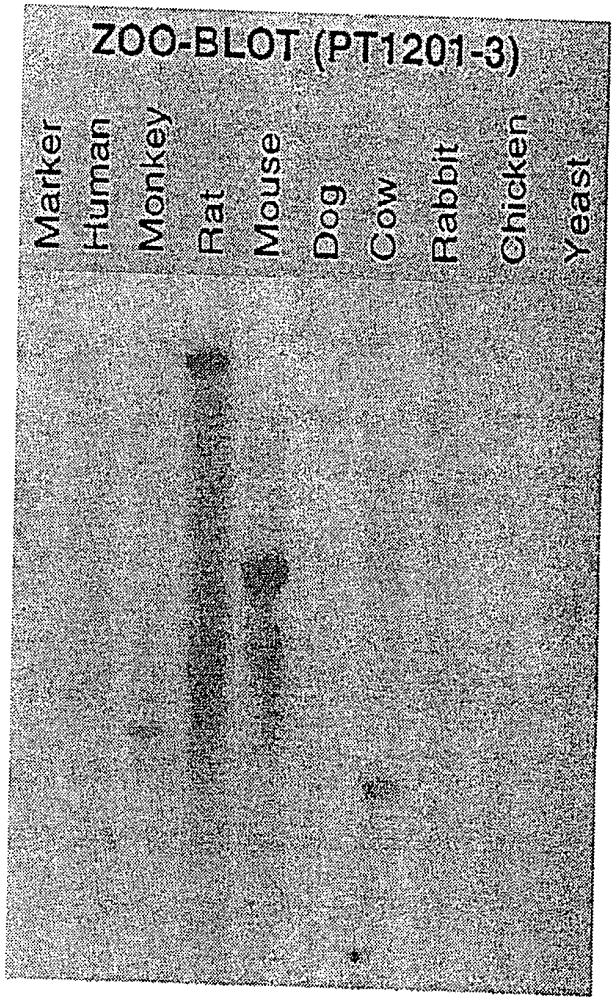
ZOO-BLOT (PT1201-3)
Marker
Human
Monkey
Rat
Mouse
Dog
Cow
Rabbit
Chicken
Yeast
M 1 2 3 4 5 6 7 8 9

FIG. 7B

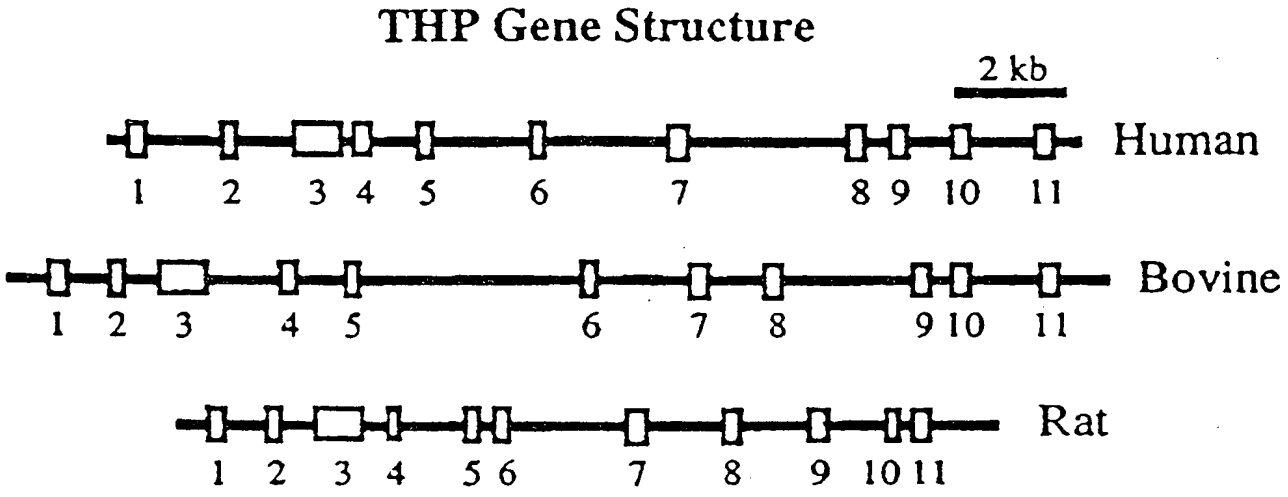
THP Gene Structure
2 kb
Human
1 2 3 4 5 6 7 8 9 10 11
Bovine
1 2 3 4 5 6 7 8 9 10 11
Rat
1 2 3 4 5 6 7 8 9 10 11

FIG.8

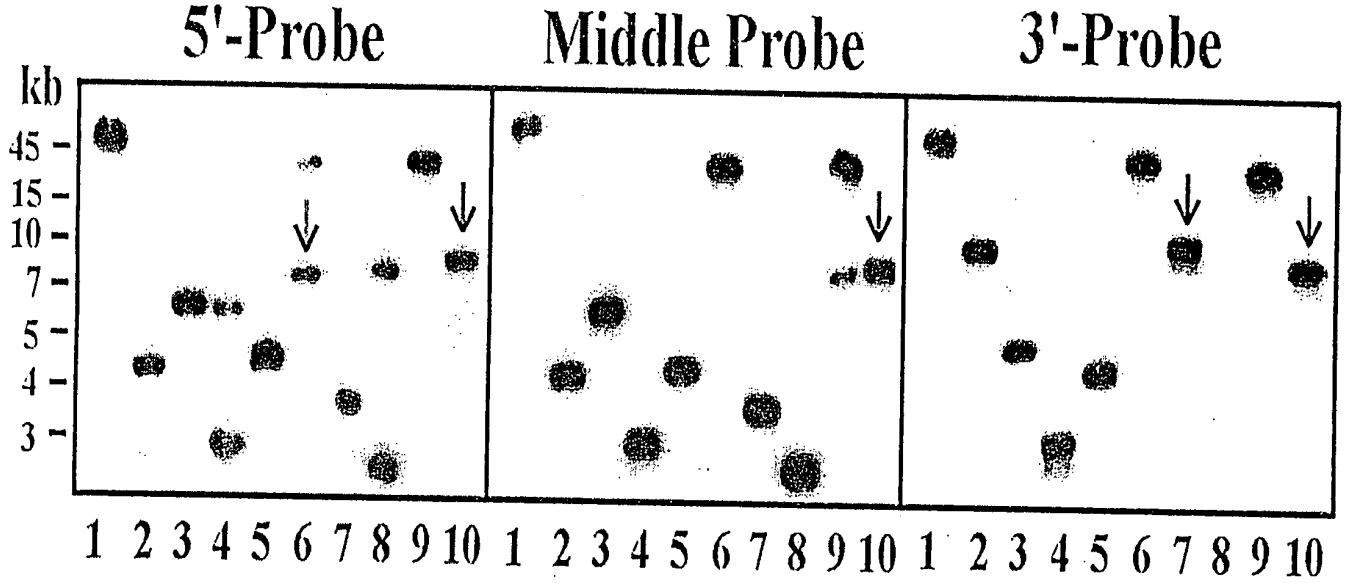
5'-Probe
Middle Probe
3'-Probe
kb
45
15
10
7
5
4
3
1 2 3 4 5 6 7 8 9 10 1 2 3 4 5 6 7 8 9 10 1 2 3 4 5 6 7 8 9 10

FIG.9

```
   1  GGGG/GGGCCC TCGGGAGTTT GGCTAAGTCT TGCAAATGAG CTGTGATGAC
      polycloning site of pBS
  51  AGGTTTGCGC CATATGAGAT CCAGTGACAA GCTCATCTCT AGATGTCTGC
 101  ATACCAATAA GTGACCCATC ATTATGCAAT CAGGCCGGAC TCATCCTCTG
 151  TGGCTTTGTC TCTTACTACT GTAAACTTGA TAACCTATAT GATTTTACCC
 201  ATTTCCCCTC CATGGCACTC AACTCTCCTC TTCCTATGTG ACCCTACTTA
 251  TGTCCTATGT GACTCCAGCT GCTTCCTTTG ATGAGAGCCA TCCTGTTCTT
          JP.S3
 301  TCTATGTGAC TCTGCTCACT TCTTCCACGT GACTCCACCA ATCTGTCTAC
 351  ATTGCAGAGT CACTCACAGT TTCTTGAGAG CAGAAGACTC AGAACTGATC
 401  TGTCCTCAAT GTCCTCCCTA CACTTTCTCC TCATAATCCA CATATCTAAA
 451  GCTATAGAGA TAATTTCATG CACTATAGCT TTCAGTACTA TCGTATCTAC
 501  TGTCTCTACC CTGTAACTGG TATCTTCATG ACATCTCGAA TATTTCCAAT
 551  TTCTCTATTG CTGCAAAGTC TTGAGAAGTC TAGTCTTATG GATCTCCTTT
 601  TCTCCTCAGG TCTCCTGGTC TCCACACACC ATTCACACTT CTTGAATATT
        JP.S4
 651  CTTTGAACAT AACAAATTCT CTCCATGGGT TTGTTCCCTC TACCCAAATT
 701  CATGCCTTCA GGATACTTAC TCTGCCCCAT CTTCACTCAT CTCTGCTTTG
 751  GTCATTCAAA TCTCAAATGT AGCCATTTCT AAAAGGCTCT CCAAGAGAAT
 801  AATATTTGAA AGCATTTTGC TATTCTATCA AGTGATCATA CAATGTCTGC
 851  TCCTGCCACC ACCATGACCA TCCCCATGAA TACAGACACT GCCTTCTTAG
        JP.S5
 901  TGTTTGCTGT ATGTGTTCTG TGTGGTACAT TGTAGATAAA TGCTGTAATA
 951  AACATCTGTG GAGCAAATTG AATCATCAGA TAGCACCCTC TCTCTGAGAG
1001  GCATGATCTC ATGGTTATCC CCAAAGCATG AGGTAAGGAC ATTATCCCAG
1051  GTCCATGCTG GTTTCCGTAT TGATTGTTTC TAACACAAAC TTAATAGATT
1101  AAAACAGCAC GGATTTATTC TCACATGTTT TGAGACGCCA GAAATCTGAC
```

FIG.10A

1151 ACCAGTTTCA ATGTTTAGAC TTGATGCACA CCTGTAATTC TGGTACTTAG

1201 GAGGCAGATG CAGGGGGACT ATGATTTAAA GCCCATTTTT AAGCTGCTGG

1251 GTGAGAACCT GTCTTGATTT TTTTTTCACA TTGGGCTAAA AGTCAAGGAT

1301 CATCAGGGTT GGTGCATTCT GGAAGAAACC TTTGCCTTGC AGCTTCCCAG

1351 AGGGCCGCCA GCATTCCTTG GCTTGTGTTT GGTCCTGGAA TCACTGTGAC

1401 CTTATGCTCC ATCCTCACAT TCCCTCTGCA TTTATCCTCT AAGCACCGGT

JP.S6

1451 GTGCTTGTAT CCAACCTTTA GGAGCCCCAT AGATCCCCCA TTTCTCCTCG

1501 ACTTAATCAC ACCTGTATAA GTACTTTTCA CTCTGCAAAG CAATATTTGT

1551 GGGTCCAAGG GATTAGGATG TGGGTATATT TGTGGGGTGT CATTATTCAA

1601 TGCTTCATAT TTACACTGTT TCTCTGTTTC ACTTTATTGG GGTACTTGAA

1651 CTTCTAAGAA GAACTGAGGG GTATTGTTGT AGGAACTAAA TTCCCCCATG

1701 GACCTCTGTG CTTTCCACCT ATCACACAAG ACAGAGGGTA TTTGTATTTT

1751 TAGATCCCCA GAAGAAATTC CCACTCTCAA CCCTCCATCC CTGACTTGCT

1801 CACATCTAGA TGAAGCAGGG AACAGCCTGA GNCCTGGAAC TCACTGGAGC

1851 CAGATGACTC TATGGAGTTA GGTTTTAGTA TTCAAGACAC GATGCAAGAC

1901 TCACCTGCCT TCCCCTCACA GACATGTGGC TGCCTGTCAA AGGTGGGGCC

1951 ATGGGGCTGC TGAGACTAAG TCACGTGGAC AGCGCCCATG ACAAGCAGTG

JP.S7

2001 ACATGGAGAC CAAGGCTGCA GTGTGCATGC TCCACAGGTG CACCTGAAGC

2051 CTCAGAGACG GGAAGAGGAG AGGGAGCAGA AAGATGGGGT ACAGATACCC

2101 CTCTGTTAGG AAGGGCTTCA AAACCGTCTT CTAAGTTTTT GATCCTTTTA

2151 AATGTATCCA CCTGTCACTT GACCCTCTCC TGCTCTGTCT GATCAGCTTC

2201 TCAAAACCCT TCATCCCCTT AACTCCACCC TACTGAAAAA AGATGAAACC

2251 ACTTGTCAAT ATAAACCTCA ACAGCTAAGC ATGGAATACT GTTAACCCCT

2301 CAAGACATAA AGCTGACTGA AGGGATAAGT TTGAAAAAAA TGGGCTTCAG

2351 TTTGCACTAG CTAAGTATGT AACCTTGAAG ATATTACTCA GTTTCTCTGA

2401 ACTTCAGTCT GCTCTCCTAT TTATTGACAA CATGTAAGAG CACATACCGG

2451 GCATTTCTTG TCACCAAATG AAGTTTCCAG TACCAGGAAT GGGTTATATC

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FIG.10B

2501 TAATCGAGTT GTTGGCCAAA GGAGTTCCAT GGAAACTCCC AAACAATCCA

2551 GGCTATTGGC AAGACTTTTG ATGTCTCTCC ACAAACTGAC AGCAACTGTT

2601 GAAAGACAAT ACCTACACAG CTCACTGAAC ACAGAGAAGC TGAGTTGGTG

2651 CCTACATAAA TCCTCTAGCT CTATGAAGGT CCATAATGGT ATTCATGGCC

2701 CTAGAAGATA CTCTTCCCTC CACCAAAGGA GAAATGTAAA CACTAAGCCA

2751 GCCATAAACC CTTTGGTCTG TTAGAGTGGC CTGCCTGCAA GTTCTGCTGG

2801 TGTAATAATG GCACAGAGCT TGTAGGAGTA ACCAAACAAT ATCTGATAGG

2851 TTAAGGCCCA CTCCATGAGA TCAAACCCAG ACCTAACAAC ACTTGGGTGG

2901 ATGAGAACCC GAGACCAGAT AGGCCAGGGA CCTATGGGAA AACTAAACAT

2951 GACTGTTCTG CTAAAAGAAC CTACCAATAA AATAGCTCCT AGTGACATTC

3001 TGCCATATTT ATAGATCAGT TCCTTGTTCA TCCATCATCA GAAAACTTCC

JP.AS14

3051 TCTTCAGTAG ATAGAAACAA ATATAGAGCC CACAGCCAGA TAATATCCAG

3101 AGAGTGAGAT ACCCTGGAAC ACTCAGCTCT AAAAGGGATG TCTCCATCAA

3151 CCCCCCCCCC CCCCACCTTT CAGGACTCAT GAAACCCTCC AGAAGACGAG

3201 TCAGAAAGAG TGTAAGATCC AGAAGGGATG GAGGACATCC AAAACTTAAG

3251 GCCTTCAAGA CACAACTGTA AGGGAACACA TATGAACTTA GAGAGATGGT

3301 GCAGCATGCA CAGAGCCTGC ATGGGCTTGT ACCAGATGGG GTTCTAGAGC

3351 TGAAAGGAGA AATGGATAGC CACTCTGATT CCTAACCCAG AAGTGACCCC

3401 TAACTGATAG TGACTTGCAA ATAAAAAATT AGTCTTTTTT CAAAGGGAGT

3451 CTCACTGGGA AAATAAACCA CTCTAAATAG TAGACCCCAT GCCCAGCAGT

3501 AGATGGCCAA CAGAAAATGA ACTCAATGTC ATCTTTGACC TTCCTTTGTC

3551 GGAAAGCTTT TTGTTTGCTT TTTCTTACCC TACAGGTCCT TTGCATATTT

JP.AS13

3601 ATTATGGTTT CTTGTTTCAG GTTTTTAATG GAACTCCTGA GTGTGTGAAT

3651 GTGTGTGTCT CTGCATACAT GTGTGTTTCT TAAGCCCGTT CTTTTTCTTT

3701 TCTTCTCTTT ATTGTTTAAA AAAACAATTG TTCTTTATTT TATTATTATT

3751 CCTTATTTTA GACAGAAACA TTGTGGATCC AGATGGGAGA AGAGGTTGGA

3801 GGAATTGGGA GGAGTAAAGG GACAGAAACC ATAATCAGGG GGAACCATAA

FIG.10C

3851 TCAGGGAGAA CCATAATCAG GGGGAGCCAT AATCAGGGGG AGCCATAATC

3901 CAAGGGAACC ATAATCAGAA TATACTGTAT GAAAAAAATT CTATTTTCAA

3951 TAAAAAAAGA ATAAAAAAAA AACAGTCTGA CTGAAGAATA GCACTTGGTA

4001 AGTAACTCTT GTTATAACAA TCCATATCAA ATGCCCTGCC TGTGTTAGCA

4051 AGTTAAGAGA AAAGATTATT CCAAGAGATC CAAGTCTCCT TCAAAACCAA

ZT.S1

4101 GTGTGTACAG AACATTGTCT GAGGAGTAAG ATTGCATTTG GCAACATGCA

4151 TGTCTTTAAT GGTGTGGAGA ATTTCAGTGG AGTTGGCACG TCAGAAAGCA

JP.AS12

4201 CACTGGTGAA AAATGGAGAG AATAGATATA TCCTTTGAGA AATTTGGTCT

4251 CAAAAAGTAG GGTATCAAAT TACTTGGTGT CTGTGAGATC AATTGGTTGT

4301 CTCTGTAGGT TAGCTTACAT AGGAGACAGG AATAAGTGAA GGAGAGAAGG

4351 GAGGACATTG GAGCACCCAA GGAGAGAGGG ACCTTCCTCC TAAAAGTGAA

4401 TGAGGTGGCC TTCATTCCAA GGAGAAGAGA TTCAGGTCGC CCGGGAAGAT

4451 GAGGGACCAA CATCCACAAG GAATGGCAGG AAGTCATCCT GTGTGCATAA

4501 ATGGAGAGAG GGGGTCAAAG ATGGAGCAAA GAAGGATGAG CAAGAAAATG

4551 GTGGATGTGG ATACTCTGAG GATGGCCTGG CTGTGGTGAG CAAAATGTGG

4601 GCAAAGTGGC ACTCCATGAA CAAGACAGCT TGCTCTGTTT GCAGATCCTT

4651 AAATAAAGGC ACATGGCATG CCATGGAGGC TAGGGGAGTG GAGGGGAAAG

4701 GTATATAGAT AGATGCAGAA GTACCAGAGG AGCCAGGAAG GACAGGAGTA

4751 GGAGGGACAG GTTTGCACAA GGCTTTGTCC TCTCCCCACC AGCTCTCTCT

JP.AS11

4801 CCCTTCTGTA TATGCACATA CACAGTGAGC TAGTGTGCAT ATGTGTGCAC

4851 ATATGCATGT GATGAACAGA GGCCAGTCTT GGGTGTCAGT CTTCAGGCCC

4901 TATCTACCTT GTTTTTGAGA CAATCTCACT TGAGTGAGTT GAGTGACTCT

4951 CCTAGTATTC TACAGAGGTT TCCTCAGGTG GGGAGGAATG GGTGGGAGAA

5001 GCAAATTTAA GACTGGTTGA TTTCTTGAAT TTCAGTGGGC TTGGGAAATA

5051 GCAGCTATAT ATTCAGTTTC CTCGTTCCTG GCTGGCTTCC TGGGGTGATC

5101 AGAGCAGAGT ATAGTAGCCC TGTGTGGCAG TCACACCAAG CAGACAGAAG

5151 ATAGGGCATG GCTCTGGTGT GGCTGGTAGA CATAGGAAAG GATCCTTGTA

5,905,024

FIG.10D

5201 GCAAGATGTT TGCCATCTCC AGAGACTTAG ACAGCCCAGG AAAGTTTGTC

5251 CTCCCAGGAC CAGCCAGCAC TGAGACTGGA ATGCATCAAA TCCAGAGACC

JP.AS10

5301 AGAAAGCACG GTGCTAGCAC TTAGGAAGAG ACACTAGCCC AAAGTCTCCT

5351 TGCTCCTGCC TAAAGCTTTG CCAATTCTGC AAACCTTGAA AAATTAGCAT

5401 CTTTAAATTC AGAAGGGATA CAAGAAGAGA ACTTACATGG GACCTTGTAA

5451 AAAAGCATAG GGCATCAGTA ACTAAAGTTA CAAAGATAAC AATCAGTGGT

ZT.S2

5501 GAGTGAACAA AGGACATGGC CATGTTTTTT TTGTTATGAA ACACACGCAC

5551 AGGCACAGGC ACTCACGTGT GCGCACGCGC GCACACACAC ACACGCGCAC

5601 ACACACACAC ACGCATGCAC ACATGCACCA CACACAAACT GCAAAAGTGA

5651 ATAAAAAGAT ATTTCTCACT TTGGCAAAGT GGATGGAAAG TTGATCAAAA

5701 TGAAAGTTAT ACTCAGAACT ATTTTGTACT AGAGGGAGGT TATAAATTAT

JP.AS9

5751 TGTTATTGTT ATATTCTATT TTACTGTTTG TGGCAGCCTA AGTTGGTCTT

5801 GAACTCACTA TGAAGCTAGC AATGACCTTG AGCTTCTGAT CCTTATATCT

5851 ACACTCTCAA GTGCCCAGAT TATAAGTGTG CACCACTATA CTCAGTTTAT

5901 GCTGTGCTAA GGACTAAGCC CAATTATACA AACACACACA CATATATACA

5951 CACATACACA CACACACACA CGTATATATA TGTATATATA TATACATACA

6001 TACACACACA CACACACATA TATGTAAAAT TTGGGAAGAT ATATCAATCT

6051 TCTTTAAAGT ACATGCTACT TTGGTCCAAA ACTTTCACTT TTAGGAAGTT

6101 AAGAAGGAAG AGACAGAATA AGAGATGTCC CAAGAAAGTC AGTGTGGTTG

6151 TCTTAGTTAT GCTTCCTGCT CAGTCAATGT TTCAGATTTT TCTCAGCACA

JP.AS8

6201 ATGACATCTA TTCTATCAAG TTTTTGATAA CTCTTTACAT GGGACTGGGT

6251 GTGGCTTGTG GCTCTAGCTA TTTCTATTTG TGACTGCCTA TCAGCAAAGC

6301 ATCCACTTCA GACTTTGACT CAAACATCAC CAAGTATTCC CACTTGCATT

6351 GTCTCTGTTA ACCAGCATCA CTGTTCACAG GGCAGGGCAT CACATCTCAC

6401 AAAGGGAAAG GGAAAGGGAA GAGTTAAATT CCCTGGGATA CTAGTCACGG

6451 TGGACTCAGG CAAACAGCCT CTTCAATTGT AAGATGATTC CCTAGTCCAA

JP.AS6

6501 GGACCCTCTA CTGTTTGGAC TCCAGTCTTG TCTGACAGAG GTCCAGTTCA

FIG.10E

US 2003/0082530 A1

6551 GGAGTGTCCA GATGGTCTGA TAACCTGATG CCATTCTCAG AGACTCTTTC

6601 CTGTCTGGAA TCTAGTGAGG AGGACTTATC TGGTGAAGCT GTCCTTTAGA

6651 ACAGGAGTGT GTTCCAGTCT TCAAAGCAAA CATTCCTTTT ATCCTAACAC

6701 AGTCTGACTT CAGATATACT GTCTTTTTCC TGGCTCCTTG GGCTTAGGTC

6751 TACCTTGTCC TTGCCCAGGT CCAAGAAAAG GCCCAGAACC TTGGCACTGT

6801 TTTGCCAGTT AATGTCTAAC TGAGGAATGT CTTGCTGCCA AAAGGTGAAA

6851 ACAGAGACCT TGTATTTCCA GGCACAGGTG TGACCCCAAT GTCAATCATT

6901 TTGTGTCTAA CTCCCAGGGG AAAAACTAAC AACAACAGAC TCATGGCTTG

ZT.S3

6951 GAAAAGGTGA ATTCTATGCC AAAAGGGAAG GAAAGTTCTA CCCCCACAGA

ZT.S4

7001 AACAATCTCA GAGGGCAGAA GCAGAGAATA ATCTGAGGGA GAGGGCCAGC

7051 CAAGGGCAGG CAAGTATATA TTGATCACAG GCACTTACTT GTGA**ATGGAC**

EXON 1

7101 **CAGTCCTGTC CTGG**GTTCAG GTAAGGCTGT ATGAAACTGT CACCCCCATA

JP.AS15

7151 TCCACTTCTC CTCTATCTAA TCCCATTATA TTTCAGGGAG GTTGTGGTAG

JP.AS4

7201 AAGCTTAGCT TCTGGACACT GGGGTCCCAT GCTAACCTTC ATGGCATCCT

7251 GGTATGCTGC TGTAAAACCT AGGGTAATGC TTGCATCCAT CTGGAATTAT

7301 TTCACCTGTT GCAACCACAA TCATTTTGAA AATACTAGTA TGTATTATAG

7351 TTATGTATGT ATATAGAGTT AATCATCTCT AAAGCTCCTT ATCTTTTGCC

7401 ATTTCTTTAC ATGAGTTGTA TGAAGATGTA GACGATATTC ATTATTCTCT

7451 TTGGTATCTA GCACCTTGTT TGGCACATAA TACTACTCAA TAAGGGTTTG

7501 TTGAATGAAT AAGTAGGTGA GAGCAAATTG TAAGTTCAGG TAATCACGAA

7551 CTTCCTGTAA AACTCCAAGG CTGCCTCCAG TAAGGTATAA GTCCTGAGTG

7601 AGCCTTTCCC CATCTTGCAA CTTTTTGCTC CAAATGAAAG ACTCAGTTCT

7651 TCAAAATGTG CAGCACATGG AGGTTTGCGA CATAGGGGTG TATTCACAGA

7701 GGCTTCGGAA GCCCACCAAA CCTACAGTTA GATCACTGTA CAGTCTTCCT

JP.AS2

7751 TTTACATACA AGCTGTGCCT CCTGGTNTAC ATCCATGCTG TTTTCTGATC

7801 CATATAGAGG GTACACAACA AAAGCATTTC TTCTGTCTAT AGGGAAGCAA

7851 ATTAGATCAT GCATGTGCCT CACCCACCTC TGTTCTCATG AT**TTCAGGCA**

FIG.10F

EXON 2

7901 **TCAGAAACAC AAGGGAAATC CAAAGTACCT AACCCATCCT TGCCTTTGGG**

7951 **CAGGTGTTTC CAGGACAGAG GGCAGAGTGT AAAGGATGGG GATCCCTTTG**

8001 **ACCTGGATGC TGCTGGTAAT GATGGTAACC TCCTGGTTCA CTCTGGCTGA**

8051 **AGCCAGTAAC TCAACAGAAG CGA**GTAAGTG TGTGTGTGTG TGTGTGTGTG

8101 TGTGTGTGTG TGTGTAGAGA AATGTTCCCT TTGCAGAAGC AATCTTAATC

JP.S1

8151 CCTCTTTTAG CACACTTGAT GTGATCTTTA TTTTAAGCCC ATTTCTCAGA

8201 TTGTAATGAG CACAGGACTC ACTTCGAAGT TTTGTTAAGA TGCAAATTCT

8251 ACTTTAGTAG GTCTAGCAAG GGG/CCCGAGA CTCTGAATTA ATAGCAGCGT

APA/KPN JUNCTION

8301 GTGGGTGATG TTTCTGGTGG GACAAGGGGC TAAAACACCT CTGAACCATT

8351 TCTGCACTTC ACGGTAAAGT CACAAGCATG CCCAGATACA TAAGAGATTT

8401 GACCCACCTC TCCTGTAAGT GTGAAGTCAT CCCATGGGGG TAGCTTTGCC

8451 TTCCACCCTG GAGTACTCTG GAATTACACT AAGTATAATT GTGAGGTCAT

8501 GGTTAAAAGC ACATGTTCTG TGGTCAGGCC ATGTGCGTGT ACCCTGTTTG

8551 ACAACTGGCT TGCTCGTTCT GAATGTCAAT ATTCTTTTCT GTAAATGAAG

8601 AAAATGAAAA TGGGTTCCAG CGGCAGGGGG TGTGCCCTGG GGAGGATTCG

8651 CTAAACTCTA GACTGAAAAG TCAATGAATA GAGGACTCCA CTCAGGGGAG

8701 CTCGGATGGG TGTGTTTTGA AGGTGCCAAC AACTTAACAA GTCCAGAAAA

8751 GCAAGAAAGT ATGGGCAGGG GCACCTGCCA GCTGCAGGGA TTCTGAAGCT

JP.AS5

8801 GGGCTCTTCT GTCCGCAG**GA CGGTGTTCTG AATGCCACAA CAACGCCACC**

EXON 3

8851 **TGCACGGTGG ATGGTGTGGT CACAACGTGC TCCTGCCAGA CCGGCTTCAC**

8901 **TGGTGATGGG CTGGTGTGTG AGGACATGGA TGAGTGTGCT ACCCCATGGA**

8951 **CTCACAACTG CTCCAACAGC AGCTGTGTGA ACACCCCGGG CTCGTTTAAG**

9001 **TGCTCCTGTC AGGATGGTTT TCGTCTGACG CCTGAGCTGA GCTGCACTGA**

9051 **TGTGGATGAG TGCTCAGAGC AGGGGCTCAG TAACTGTCAT GCCCTGGCCA**

9101 **CCTGTGTCAA CACAGAAGGC GACTACTTGT GCGTGTGTCC CGAGGGCTTT**

9151 **ACAGGGGATG GTTGGTACTG TGAGTGCTCC CCAGGCTCCT GTGAGCCAGG**

FIG.10G

9201 ACTGGACTGC TTGCCCCAGG GCCCGGATGG AAAGCTGGTG TGTCAAGACC

9251 CCTGCAATAC ATATGAGACC CTGACTGAGT ACTGGCGCAG CACAGAGTAT

9301 GGTGTGGGCT ACTCCTGTGA CGCGGGTCTG CACGGCTGGT ACCGG

POLYCLONING SITE OF pBS

FIG.10H

0950450 "0950950

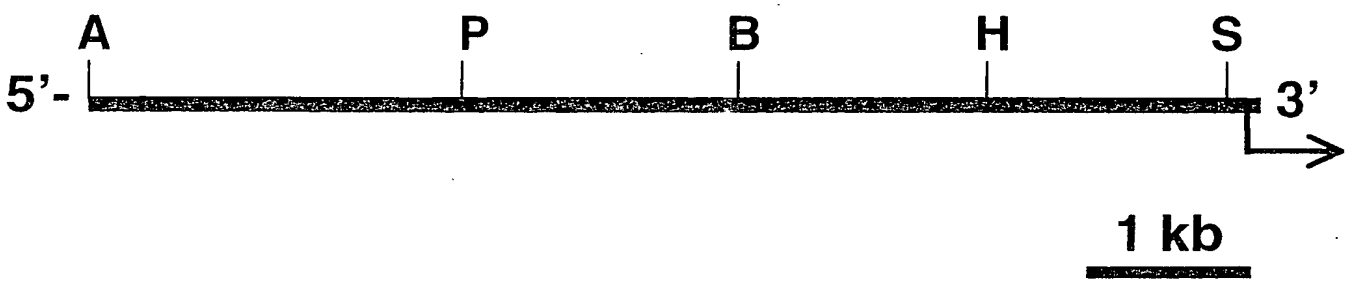

FIG.11

```
  1  TACTGGCGCA GCACAGAGTA CGGCTCCGGC TACGTCTGTG ATGTCAGTCT
                                        <-AS14
 51  GGGCGGCTGG TACCGCTTCG TGGGCCAGGG CGGCGTGCGC CTGCCCGAGA
101  CCTGCGTGCC CGTCCTGCAC TGCAACACGG CCGCGCCTAT GTGGCTCAAC
                                        <-AS15
151  GGCACGCACC CATCGAGCGA CGAGGGCATC GTGAACCGCG TGGCCTGTGC
201  GCACTGGAGC GGCGACTGCT GCCTGTGGGA CGCGCCTGTC CAAGTGAAGG
251  CCTGTGCCGG CGGCTACTAC GTGTACAACC TGACAGAGCC CCCTGAG
     <-AS17
```

FIG.12

```
  1  ACTATAGGGC ACGCGTGGTC GACGGCCCGG GCTGGTAAAT CTTAAAAAAA
                                  AS1
 51  AAAAAAAACA AAAAGAACAT CACTAAGCCC CCCTGCCCTG GCACTTTATT
                                        AS2
101  GGAAGGTCAA GAACACACTC AACCACACAA GAGATGTGAA CATACCTGTG
                    AS3
151  TGGTACCCAA AGACATCCCC TTTCACACAT ACATGACCCT TCCATTGGGT
                AS4                                  AS5
201  TGCACATTGC TGTTAGCTTT TTGTTGGAGA AGGGAGCTAG ACACCTCTAC
251  ACAACCCCCA ACTGGAGTTC TCTGGAACAG AGTAAATACC ATCGTGTCAT
301  CATGGAGCGC ACACACACTG TGGTCCTGCA ACCTCGATTT GTGTCCTGGC
351  TCTGCTGCTT ACCAATGAAG CAAGTAGCTT AAACCTTCTG AATCTCAAGT
401  TTCCTCACCC TCAAACTATA GCTAAATACA AAAGTCATTT CCCAGGGCCA
451  CTGGAGAGGA TTCTATCAGA TAATGGATAG AAGATGCCTA TCCCAGTGTT
501  TGACATATCC TAAGTGCTTA ATACACGAGA GCTCACCATC TTTACTGGTA
551  TTATTGCACA GAGAAACACA CAAAGTGTCA GTGCCCCTGC TAGGTAGAGA
601  GGGANGCANG GNAAGGAGAT CTGAGCAAAA GGCATAGAAT ATATCAAGCT
651  GGG
```

FIG.13A

0050050.050000

```
  1  CGGGGGAAGG TTTATTTTGT TTCTTTTCAA AGGGGGTCTT GNTCTGTCTC
 51  AAAGACCNTA AGGACCATGA AAAAATCTCT TTGTNAAAAG TGCCAAGCGG
101  TCCCCACTCT GAATCTGGGC TTTTCTGCCT GCAGAAAGCT GCTCTGAATG
151  TCACGCCAAT GCCACTTGTA CGGTGGACGG GGCTTGCCAC GACCTGCGCC
201  TGCCAGGAGG GCTTCACTGC GACGGCCTCG AATGTGCGGA TCTGGATGAA
251  TGCGCCATTC TGGGGGCGCA CAACTGCTCC GCCACCAACA GCTGCGTGAA
301  CGCGCTGGGC TCCTACACAT GCGTCTGCCC TGAAGGTTTC CTCCTGAGCT
351  CGGAGCTCGG CTGCGAGGAT GTGGACGAGT GTGCAGAGCC AGGGCTCAGC
401  CGCTGCCACG CCCTGGCCAC CTGCATCAAT GGCGAGGGCA ACTACTCATG
451  CGTGTGTCCC GCGGGCTACG TGGGGGACGG GAGGCACTGT GAGTGTTCCC
501  CGGGCTCCTG CGGGCCTGGG CTAGACTGCG TGCGGGAGGG TGACGCGCTA
551  GTGTGCGCTG ACCCGTGCCA GGCGCACCAC ATCCTGGACG AATACTGGCG
601  CAGCACAGAG TACGGCTCCG GCTACGTCTG TGATGTCAGT CTGGGCGGCT
651  GGTAC
```

FIG.13B

```
  1  ACTATAGGGC ACGCGTGGTC GACGGCCCGG GCTGGTAAAG ACACCCAGAC
 51  TTAGGTTTTG ACAGAGCCTC ATGTTCACCA ACCAGAAATG ACATTCACCA
101  CCTAGGATTG AGAAAAAGAA TATTAGGAAC TTTTATTTTC TTCTGAAGTT
151  ATAGCAAAGA AAGGGGAAAA AAAAAAACAT TCTTATGGGG GATAAACGGG
201  CAAAGGATAC AAACAGTTCA GAAAAGAATA AATAGTAAGC AAATGAAAAG
251  ATAACTTCCT TTTTCATCAA AGAACCGCAA AAGTAAATAA TGATAAGATG
301  TTTCTCACTT TTCCACAAAG ATGAAAGTTA ATGCCCAGGG TGGCTGAGTA
351  CTGTGCTGGG ATTGTGAACT AACTGTTATA GATCTCTCTG GGGTGCTGTT
401  TGGGAAGAAA CATCGCTGAA AACTGAGCTA CCTCTTTTCC TATGAAATTC
451  CCCTGAGGAG GTGAGTGAGC CGCTGCTGAT CGTCACCCGA GCACTAGGCC
501  AGACAGAAGG AGAAAGCCCT CAAAGAGGCA ATGCTGTGGA TCACTGTCAT
551  ATTTCCTGCT CAGCCTGAGT TCACATGTGC CTGATTTTTC TCAATATGGC
601  ATTGCCATTA ACGTGGAATT AGGTCAGGAG ACCTAAGGCT GAACCAAGCC
651  CTGTCATTCT CTGCCCCATG ACTGCGCATC ACCAAAACAG CATCGGCAGT
701  GACTTCCACA GATGGTACCA TTGCTATATG CCTTAACTTG CATCATCTCC
751  TTTAATGGCC ATAACAATTC TAGGACACGG GTATTCTTGT TTTACAGATG
801  ATGAAAATTA CCTCTGGAAG GAAAATTACT GGCACACAAA AAACGCTGAC
851  CAGGATTCAG ATAGACTGAC TCCAAAGTCA GTCTGTTCAT CTACAAAATT
901  ATCTACTTCT CAAGGACCTT CCTTCATGGG AATTCAAATT TCTTGATTCA
951  CAGAGCATCT GGTCCAATGA TGTCTGAATT ATCTGCTGTC TCTGACCTTC
```

FIG.14A

05605045.050502

```
1001  AGCCATTCTC AGCTCCTTTC CTGATCACAT TGGGACCCCA GGGGAGCTGG
1051  CTGAATCTGT GAGGATGGCA TTTGCTTTGG AATTAAGTGG CCACAAGTAC
1101  ACATCCTGGT GGGGACGATG AGCACCCCTT TTCTCCTGGA GCAGCCTGGC
1151  TTCAGATTCT GGCCTCTGCT TGGCTCCACT TTGTGCTTTT CAATGACCAA
1201  GAAAATCCCA GGCCCTTGGA ATTGTTTACT CAGTTAATTT CTAACTAAAG
1251  AACCTCTTGT TGCCAAAAGG TATAAAACAG AGCCCTTGTA GCTGTGGGCA
1301  CAGCTGTGAC CCCCATGTCA ATCATTTGGG GTCTCTACCT ATTAGGGAAA
1351  AGAACAACAA CCACCTCACA GCCTAGAAAA GGAAAACACT GTGTCAAAAG
1401  GGAAAAATAT TCCACCCCCA TTAAAATAAT TAAGAAACAG AACCAGAGGA
1451  TCATTGGAGG AGAGATTGCC AGTGGGGGAC AGATGTATAT ATATAGATAT
1501  GAAAGTCACC TACTTGTAAA AGGATTAATT CTACCTTTCT GGTTTCAGGT
1551  AAGGCTATCT GCAGCTCTCA CTTCTCCTAG CCACTTCTCC CATCTAGTCT
1601  TTGCTGGCTC CCATTCTGTT TGAAGGATGG
```

FIG.14B

```
$ type guromodulinpromoter18full.pair;1
 BESTFIT of: Guromodulinpromoter18full  check: 3852  from: 1  to: 1630

 to: mouseThppromoterfull.  check: 5595  from: 1  to: 9343

 Symbol comparison table: Gencoredisk:[Gcgcore.Data.Rundata]Swgapdna.Cmp
 CompCheck: 2335

        Gap Weight:     50      Average Match: 10.000
     Length Weight:      3   Average Mismatch: -9.000

           Quality:   1617             Length:    534
             Ratio:  3.177              Gaps:     15
 Percent Similarity: 74.385   Percent Identity: 74.385

        Match display thresholds for the alignment(s):
                    | = IDENTITY
                    : =   5
                    . =   1

 Guromodulinpromoter18full x Thppromoterfull. March 24, 2000 16:31   ..

 1121 AGCACCCCTTTTCTCCTGGAGCAGCCTGGCTTCAGA.............T 1157
      | ||  |||||| ||||     ||| ||| |||||||           |
 6677 AACATTCCTTTTATCCTAACACAGTCTGACTTCAGATATACTGTCTTTTT 6726

 1158 TCTGGCCTCT...GCTTGGCTCCACTTTGTGCTTTTCAATGACCAAGAAA 1204
       |||||  ||   |||| | || || |||| |||  | | | ||||||||
 6727 CCTGGCTCCTTGGGCTTAGGTCTACCTTGTCCTTGCCCAGGTCCAAGAAA 6776

 1205 A.TCCCAGGCCCTTGGAATTGTTTACTCAGTTAATTTCTAACTAAAGAAC 1253
      |  |||||  |||||| | |||||   |||||||| ||||||| | |||
 6777 AGGCCCAGAACCTTGGCACTGTTTTGCCAGTTAATGTCTAACTGAGGAAT 6826

 1254 CTCTTGTTGCCAAAAGGTATAAAACAGAGCCCTTGTAGCTGTGGGCACAG 1303
       ||||| ||||||||||  |||||||| ||||||| |  |||||||
 6827 GTCTTGCTGCCAAAAGGT.GAAAACAGAGACCTTGTATTTCCAGGCACAG 6875

 1304 CTGTGACCCCCATGTCAATCATTTGGGGTCTCTACCTATTAGGG...AAA 1350
       ||||||||| ||||||||||||   || |||| ||   ||||   |||
 6876 GTGTGACCCCAATGTCAATCATTT..TGTGTCTAACTCCCAGGGGAAAAA 6923

 1351 AGAACAACAACCACCTCACAGCCTAGAAAAGGAAAACACTGTGTCAAAAG 1400
       |||||||||   |||| || | ||||||| ||  || || ||||||
 6924 CTAACAACAACAGACTCATGGCTTGGAAAAGGTGAATTCTATGCCAAAAG 6973

 1401 GGAA.AAATATTCCACCCCCATTAAAATAAT.TAAGA.AACAGAACCAGA 1447
      ||||  ||  ||| ||||||| ||| ||| | |||  ||||| ||||
 6974 GGAAGGAAAGTTCTACCCCCACAGAAACAATCTCAGAGGGCAGAAGCAGA 7023

 1448 GGATCATTGGAGGAGAGATTGCCAGTGGGGGACAGATGTATATATATAGA 1497
      | || ||  |||| ||||  |||||    || |||  | |  ||||||
 7024 GAATAATCTGAGG.GAGAGGGCCAGCCAAGGGCAG..GCAAGTATATATT 7070

 1498 TATGAAAGTCACCTACTTGTAAAAGGATTAATTCTACCTTTCTGGTTTCA 1547
       || | || ||| ||||||| || |||  | | ||    | |||| ||||
 7071 GATCACAGGCACTTACTTGTGAATGGACCAGTCCT...GTCCTGGGTTCA 7117
```

FIG.15A

```
1548 GGTAAGGCTATCTGCAGCTCTCACTTCTCCTAGCCACTTCTC..CCATCT 1595
     |||||||||| | || | || ||||  | | || ||||||||||  | ||||
7118 GGTAAGGCTGTATGAAACTGTCAC.CCCCATATCCACTTCTCCTCTATCT 7166
                  .          .          .
1596 AGTCTTTGCTGGCTCCCATTCTGTTTGAAGGATG 1629
     |            ||||||| | ||| | ||| |
7167 A...........ATCCCATTATATTTCAGGGAGG 7189
```

FIG.15B

0960504.0960505

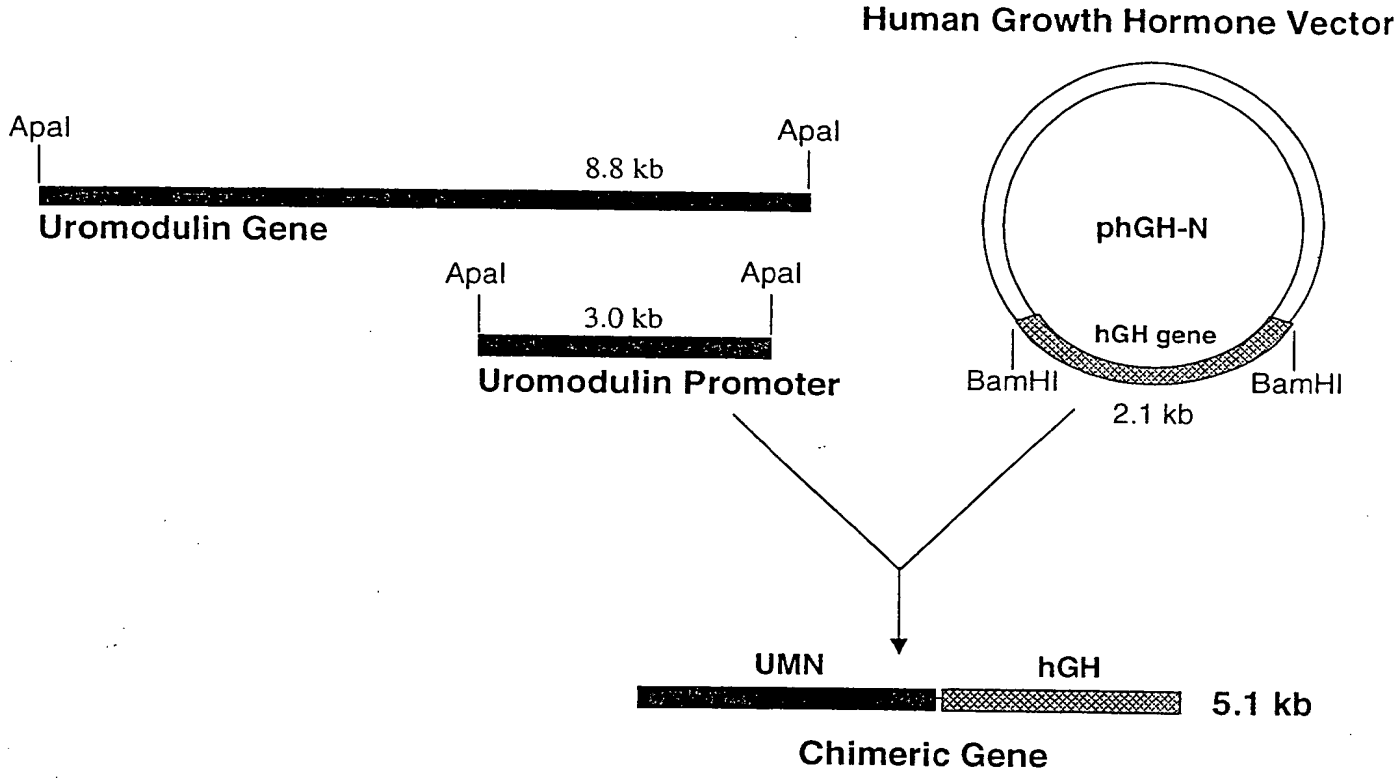
Human Growth Hormone Vector
ApaI
ApaI
8.8 kb
Uromodulin Gene
ApaI
ApaI
3.0 kb
Uromodulin Promoter
phGH-N
hGH gene
BamHI
BamHI
2.1 kb
UMN
hGH
5.1 kb
Chimeric Gene

FIG.16

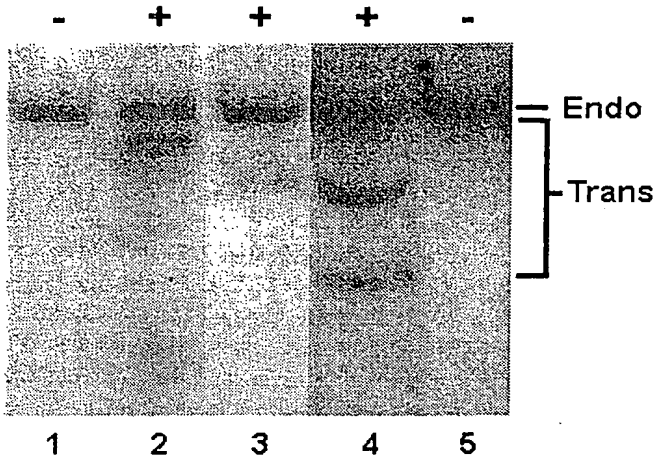
- + + + -
Endo
Trans
1 2 3 4 5

FIG.17

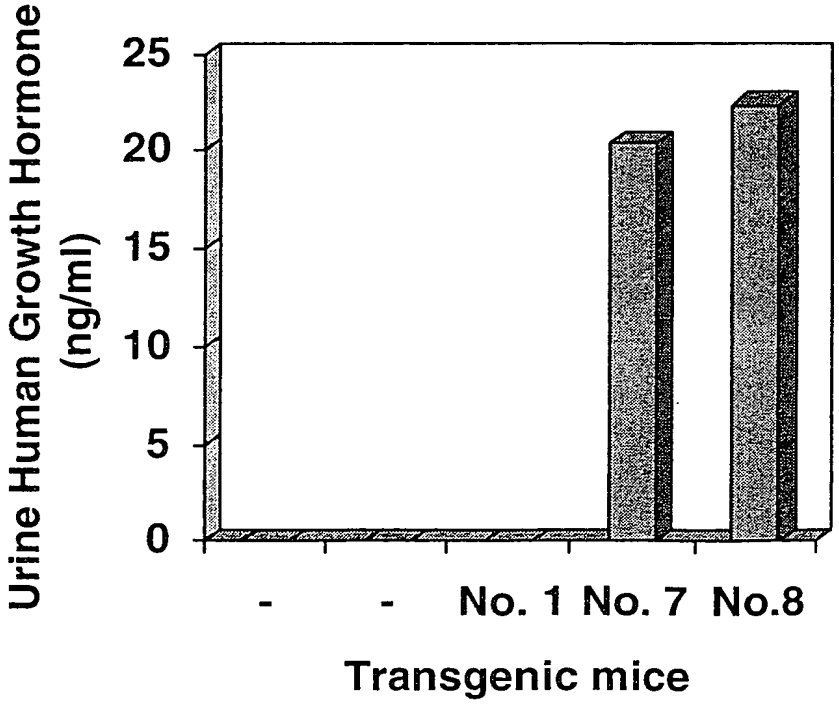
Urine Human Growth Hormone (ng/ml)
25
20
15
10
5
0
- - No. 1 No. 7 No.8
Transgenic mice

FIG.18

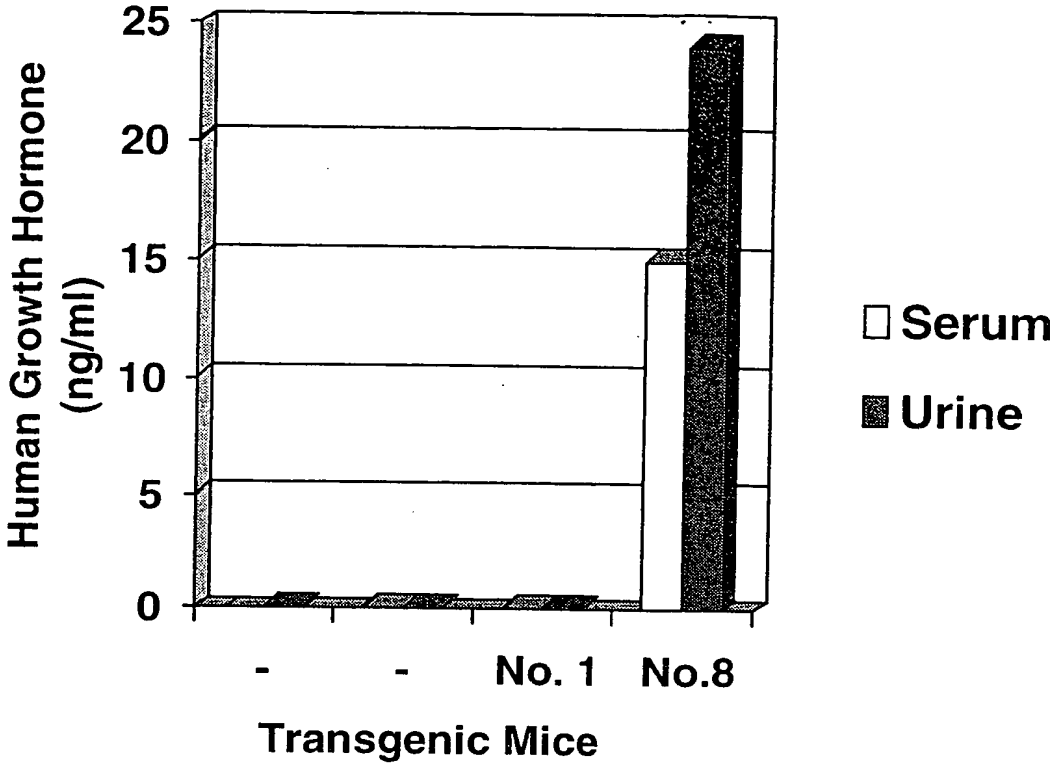
Human Growth Hormone (ng/ml)
25
20
15
10
5
0
- - No. 1 No.8
Transgenic Mice
Serum
Urine

FIG.19

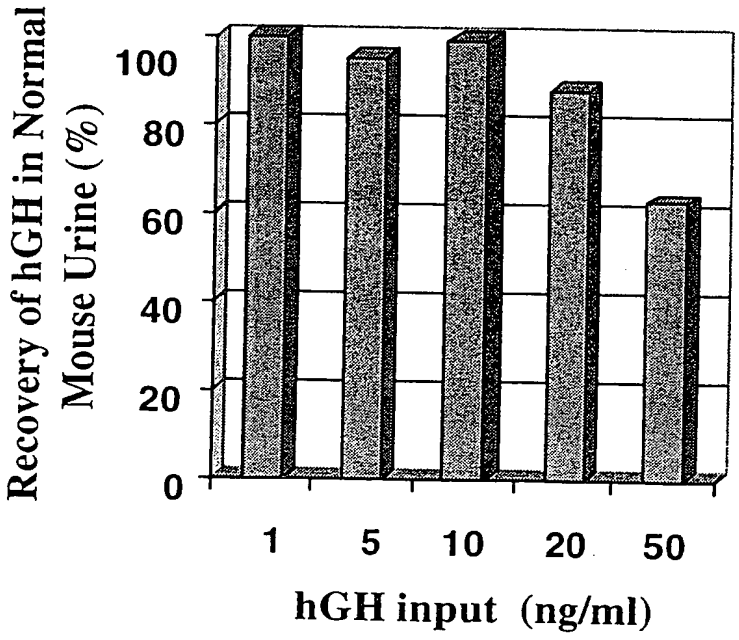
Recovery of hGH in Normal Mouse Urine (%)
100
80
60
40
20
0
1 5 10 20 50
hGH input (ng/ml)

FIG.20